

**AMENDMENTS TO THE CLAIMS:**

*Please amend claims as set forth below.*

- 1-34. (Cancelled).
35. **(Currently amended)** A transgenic mouse comprising a yeast artificial chromosome (YAC), wherein the YAC contains at least a majority of the human Ig V $\lambda$  genes of cluster A and all the human Ig J $\lambda$ - C $\lambda$  segments in germline configuration, wherein human Ig lambda genes in which the proportion of the  $\kappa$  and  $\lambda$  light chains expressed by said transgenic mouse resembles that found in humans, and exhibits relative proportions of  $\leq 60\%$   $\kappa$  light chains and  $\geq 40\%$   $\lambda$  light chains, wherein at least one endogenous  $\kappa$  light chain locus of the transgenic mouse is not disrupted.
36. **(Currently amended)** The transgenic mouse according to claim 35, wherein the YAC is comprising as a translocus a yeast artificial chromosome (YAC) of about 410 Kb, wherein the YAC contains at least a majority of the human V $\lambda$  genes of cluster A and all the human J $\lambda$ - C $\lambda$  segments in germline configuration, and wherein the translocus YAC containing human Ig segments shows high expression and is able to compete with the endogenous mouse  $\kappa$  locus.
37. **(Currently amended)** The transgenic mouse according to claim 35, comprising as a translocus a YAC of about 410 Kb, wherein the YAC contains at least a majority of the human V $\lambda$  genes of cluster A and all the human J $\lambda$ - C $\lambda$  segments in germline configuration, and wherein the mouse has one or both one of the endogenous Ig $\kappa$  alleles loci of the mouse is disrupted, and wherein the translocus YAC containing human Ig segments shows high expression.

38. (Previously presented) The transgenic mouse according to claim 35, comprising a 380 Kb region of the human immunoglobulin (Ig) λ light (L) chain locus in germline configuration, wherein the 380 Kb region resides on a yeast artificial chromosome (YAC) that accommodates the most proximal V (variable gene) λ cluster, wherein the 380 Kb regions has 15 V λ genes and all J λ- C λ segments with the 3' region, wherein the 3' region includes a downstream enhancer.
39. (Previously presented) The transgenic mouse according to claim 35, wherein the mouse includes a Hulgλ YAC that accommodates a 380 Kb region of the human λ light chain locus in authentic configuration with all Vλ genes of cluster A, the Jλ- Cλ segments and the 3' enhancer.
40. (Previously presented) The transgenic mouse according to claim 39, wherein the Hulgλ YAC is shown in Figure 1.
41. (Currently amended) A method for producing a transgenic mouse according to claim 35, comprising:
  - (a) introducing a Hulgλ YAC into murine embryonic stem[[s]] cells, wherein the Hulgλ YAC accommodates a 380 Kb region of the human λ light chain locus in germline configuration with all Vλ genes of cluster A, the Jλ- Cλ segments, and a downstream enhancer at the 3' region; and
  - (b) deriving a transgenic mouse from the cells of step (a) by blastocyte injection to form a chimeric animal and then breeding the chimeric mouse to obtain a transgenic mouse.
42. (Currently amended) The method of claim 41, wherein [[a]] the Hulgλ YAC [[of]] is about 410Kb that can accommodate a 380 Kb region (Vλ- JCλ) of the human λ light chain locus with V, J and C genes in germline configuration is introduced into said stem cells.

43. **(Currently amended)** The method according to claim 41, wherein two copies of the neomycin resistance gene (NEO<sup>r</sup>) are site-specifically integrated into the ampicillin gene on the left (centromeric) YAC arm in order to permit selection.
44. (Previously presented) The method according to claim 41, wherein YAC-containing yeast cells are fused with HM-1 embryonic stem (ES) cells and G418 resistance colonies are picked and analysed 2-3 weeks after protoplast fusion.
45. (Previously presented) The method according to claim 41, wherein ES cells containing a complete Hulgλ YAC copy are used for blastocyte injection to produce a chimeric animal.
46. (Previously presented) The method according to claim 41, wherein breeding of a chimeric animal with a Balb/c mouse results in germline transmission.
47. (Previously presented) The method according to claim 46, comprising breeding the mouse with κ<sup>-/-</sup> mice to establish lines of transgenic mice.
48. **(Currently amended)** A transgenic mouse comprising a yeast artificial chromosome (YAC), wherein the YAC contains at least a majority of the human Ig Vλ genes of cluster A and all the human Ig Jλ- Cλ segments in germline configuration, and expressing human λ light chain locus genes and endogenous κ light chain locus genes, wherein the expression of the human λ locus is equal to or greater than that of the endogenous κ light chain locus, and wherein at least one endogenous κ light chain locus of the transgenic mouse is not disrupted.
49. **(Currently amended)** The transgenic mouse ~~comprising human λ light chain genes~~ according to claim 48, wherein the mouse further comprises a human κ light chain locus and wherein expression of the human λ light chain locus is equal to or greater than that of the human κ light chain locus.

50. (Currently amended) The transgenic mouse ~~carrying human λ light chain genes~~ according to claim 48, wherein the  $\lambda$  translocus locus has been bred to homozygosity.
51. (Currently amended) The transgenic mouse ~~carrying human λ light chain genes~~ according to claim 48, wherein the rearranged variable genes in the  $\lambda$  translocus locus are subject to somatic hypermutation.
52. (Currently amended) The transgenic mouse ~~carrying human λ light chain genes~~ according to claim 48, wherein the mouse comprises ~~as a translocus~~ a yeast artificial chromosome (YAC) of greater than 100Kb which contains a proportion of the human V $\lambda$  genes proximal to the J $\lambda$ -C $\lambda$  cluster in germline configuration.
53. (Previously presented) The transgenic mouse according to claim 52, wherein the YAC includes a 380 Kb region of the human Ig $\lambda$  locus in authentic configuration with at least a majority of the V $\lambda$  genes of cluster A, J $\lambda$ -C $\lambda$  segments and a 3' enhancer.
54. (Currently amended) The transgenic mouse ~~carrying human λ light chain genes~~ according to claim 52, wherein the transgenic mouse comprises variable, joining and constant genes of the human  $\lambda$  light chain locus as a transgenic locus on a YAC, wherein B cells of said mouse rearranges said  $\lambda$  light chain genes and the mouse expresses serum immunoglobulins containing human  $\lambda$  light chains.
55. (Currently amended) The transgenic mouse ~~comprising human λ light chain genes~~ according to claim 52, wherein the  $\lambda$  translocus locus is rearranged with similar efficiency as endogenous mouse  $\kappa$  and at the same time as or before the endogenous  $\kappa$  locus.

56. **(Currently amended)** The transgenic mouse ~~comprising human λ light chain genes~~ according to claim 52, wherein one of the the endogenous κ locus loci ~~has been is~~ silenced, and the mouse expresses serum immunoglobulins containing human λ light chains.
57. **(Currently amended)** The transgenic mouse ~~carrying human λ light chain genes~~ according to claim 52, further comprising human heavy chain genes as a second transgenic locus integrated on a separate YAC, wherein the mouse expresses serum immunoglobulin molecules containing combinations of human heavy and λ light chains.
58. **(Currently amended)** The transgenic mouse ~~carrying human λ light chain genes~~ according to claim 57, wherein the second transgenic locus carries a diversity of human heavy chain constant region genes and includes μ, δ and γ genes.
59. **(Currently amended)** The transgenic mouse ~~carrying human λ light chain genes and human heavy chain genes~~ according to claim 58, wherein the heavy chain transgenic locus carries a diversity of human heavy chain constant region genes and includes μ, δ and γ genes, wherein the heavy chain constant regions genes are in authentic germline configuration.
60. **(Currently amended)** The transgenic mouse ~~carrying human λ light chain genes~~ according to claim 52, further comprising human κ light chain genes as a second transgenic light chain locus integrated on a separate YAC, wherein the mouse expresses serum immunoglobulin molecules containing human κ and λ light chains.
61. **(Currently amended)** The transgenic mouse ~~carrying human λ light chain genes~~ according to claim 52, further comprising human heavy chain genes as a second transgenic locus and human κ light chain genes as a third transgenic

locus, wherein the mouse expresses serum immunoglobulin molecules containing human heavy chains in combination with at least one of human  $\kappa$  or  $\lambda$  light chains.

62. (Currently amended) The transgenic mouse ~~carrying human  $\lambda$  light chain genes~~ according to claim 52, wherein expression of the endogenous mouse heavy and/or light chain loci ~~has been~~ are prevented and which the transgenic mouse expresses serum immunoglobulin containing human heavy and/or light chains, wherein the transgenic mouse is deficient in production of mouse immunoglobulin.